

WHAT IS CLAIMED IS:

1. A method of treating Alzheimer's disease or a dementia of vascular origin comprising administering to a mammal in need thereof a therapeutically effective amount of an endothelin antagonist.

2. The method of claim 1 wherein the endothelin antagonist comprises an endothelin-A antagonist.

3. The method of claim 2 wherein the endothelin-A antagonist comprises a specific endothelin-A antagonist.

4. The method of claim 2 wherein the endothelin-A antagonist comprises a nonspecific endothelin-A antagonist.

5. The method of claim 1 wherein the endothelin antagonist is selected from the group consisting of compounds 1 through 35 of Appendix A.

6. The method of claim 1 wherein the endothelin antagonist is selected from the group consisting of compounds 36 through 45 of Appendix C.

7. The method of claim 1 wherein the endothelin antagonist is selected from the group consisting of compounds 46 through 67 of Appendix B.

8. The method of claim 1 wherein the endothelin antagonist is selected from the group consisting of compounds 68 through 109 of Appendix D.

9. The method of claim 1 wherein the endothelin antagonist is selected from the group consisting of atrasentan, tezosentan, bosentan, sitaxsentan, enrasentan, BMS-207940, BMS-193884, BMS-182874, J-104132, VML 588/Ro 61-1790, T-0115, TAK-044, BQ-788, BQ123, YM-598, LU 135252, PD 145065, A-127722, ABT-627, A-192621, A-182086, TBC3711, BSF208075, S-0139, TBC2576, TBC3214, PD156707, PD180988, ABT-546, ABT-627, Z1611, RPR118031A, SB247083, SB217242, S-Lu302872, TPC10950, SB209670, and mixtures thereof.

10. The method of claim 1 wherein the endothelin antagonist comprises BQ123.

11. The method of claim 1 wherein the endothelin antagonist comprises an endothelin converting enzyme inhibitor.

12. The method of claim 11 wherein the endothelin converting enzyme inhibitor is selected from the group consisting of N-((1-((2(S)-(acetyl-thio)-1-oxopentyl)-amino)-1-cyclopentyl)-carbonyl-S-4-phenylphenyl-alanine methyl ester), phosphoramidon, and mixtures thereof.

13. The method of claim 1 further comprising administering a therapeutically effective amount of a second therapeutic agent useful in the treatment of Alzheimer's disease or a dementia of vascular origin.

14. The method of claim 13 wherein the second therapeutic agent comprises a cholinesterase inhibitor.

15. The method of claim 14 wherein the cholinesterase inhibitor is selected from the group consisting of tacrine, metrifonate, bethanacol, physostigmine, donepezil, rivastigmine, galantamine, and mixtures thereof.

16. The method of claim 13 wherein the second therapeutic agent comprises a statin.

17. The method of claim 16 wherein the statin is selected from the group consisting of atorvastatin, fluvastatin, lovastatin, pravastatin, and mixtures thereof.

18. The method of claim 13 wherein the second therapeutic agent is selected from the group consisting of a nonsteroidal antiinflammatory drug, memantine, CX516, AN-1792, COSNIShunt, and mixtures thereof.

19. The method of claim 13 wherein the endothelin antagonist and second therapeutic agent are administered simultaneously.

20. The method of claim 13 wherein the endothelin antagonist and second therapeutic agent are administered from a single composition.

21. The method of claim 13 wherein the endothelin antagonist and second therapeutic agent are administered from separate compositions.

22. The method of claim 13 wherein the endothelin antagonist and second therapeutic agent are administered separately.

23. The method of claim 22 wherein the endothelin antagonist is administered prior to the second therapeutic agent.

24. The method of claim 22 wherein the endothelin antagonist is administered after the second therapeutic agent.

25. The method of claim 1 wherein the mammal is a human.

26. An article of manufacture comprising:

- (a) a packaged composition comprising an endothelin antagonist;
- (b) an insert providing instructions for administration of (a) to treat Alzheimer's disease or a dementia of vascular origin in a mammal; and
- (c) a container for (a) and (b).

27. An article of manufacture comprising:

- (a) a packaged composition comprising an endothelin antagonist;
- (b) a packaged composition comprising a second therapeutic agent useful in a treatment of Alzheimer's disease or a dementia of vascular origin,
- (c) an insert providing instructions for a simultaneous or sequential administration of (a) and (b) to treat Alzheimer's disease or the dementia of vascular origin in a mammal; and
- (c) a container for (a), (b), and (c).

28. An article of manufacture comprising:

(a) a packaged composition comprising an endothelin antagonist and a second therapeutic agent useful in the treatment of Alzheimer's disease or a dementia of vascular origin;

(b) an insert providing instructions for administration of (a) to treat Alzheimer's disease or a dementia of vascular origin in a mammal; and

(c) a container for (a) and (b).

29. A composition comprising (a) an endothelin antagonist, (b) a second therapeutic agent useful in the treatment of Alzheimer's disease or a dementia of vascular origin, and (c) an optional excipient.

30. The composition of claim 29 wherein the endothelin antagonist comprises an endothelin-A antagonist.